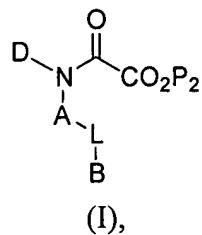


### Amendments to the Claims

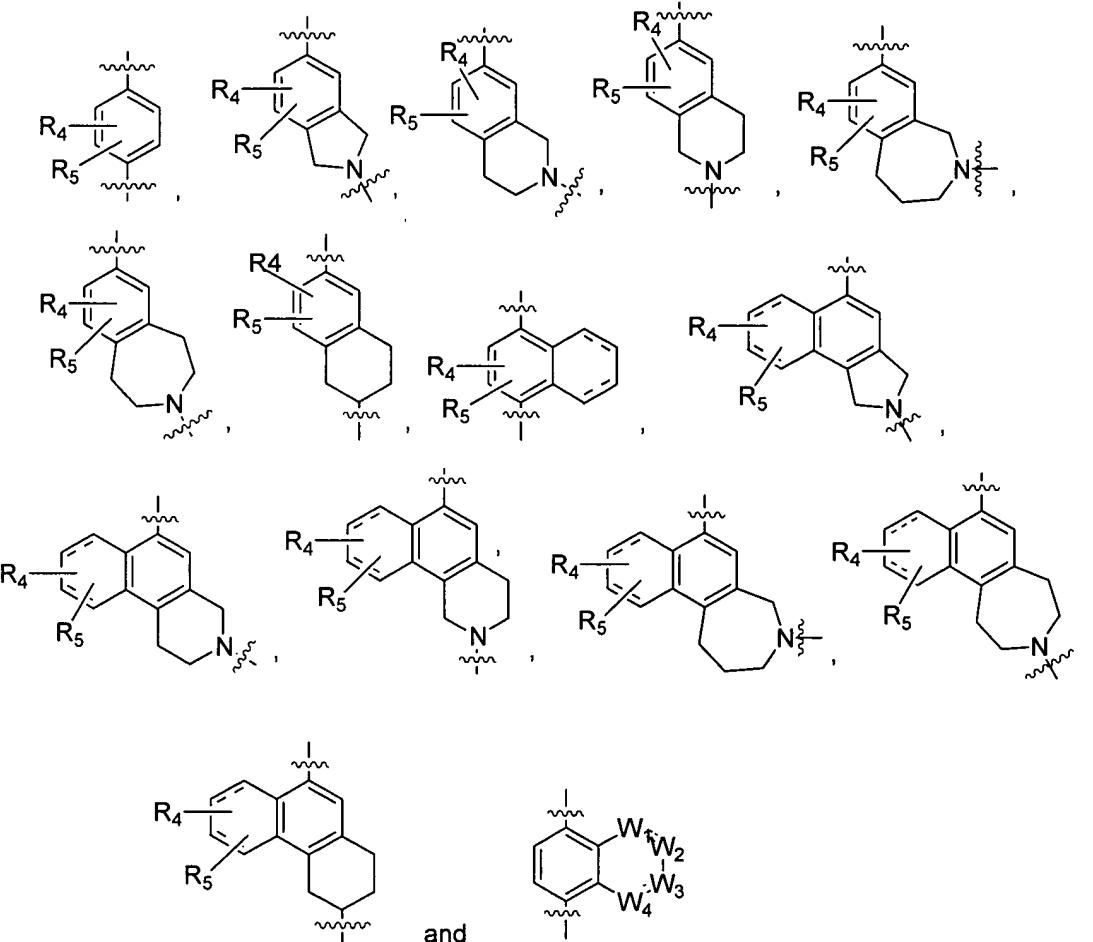
1 (Currently Amended).

A compound of formula (I)



or a therapeutically acceptable salt or prodrug thereof, wherein

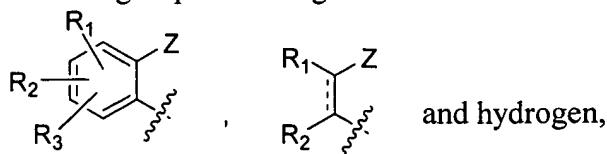
A is selected from the group consisting of



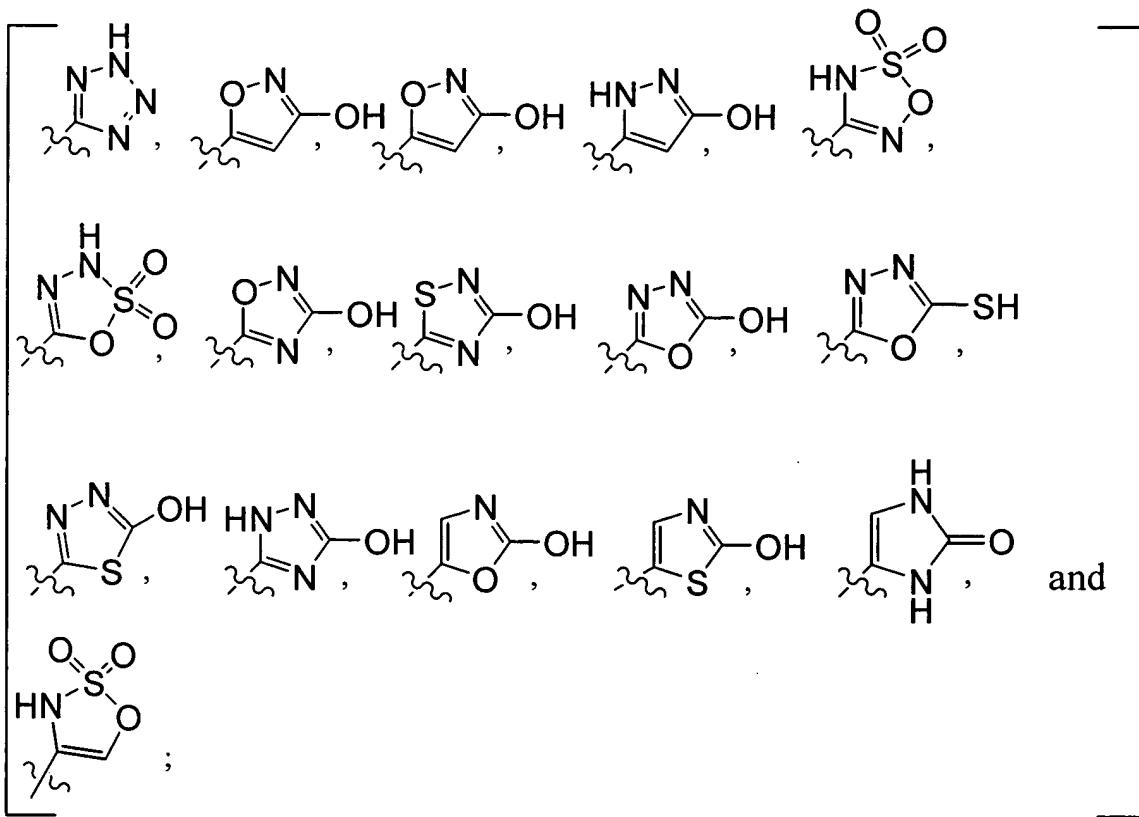
wherein the dotted line is either absent or is a single bond;

B is selected from the group consisting of hydrogen, alkyl, aryl, arylalkyl, **heteroeycle and heteroeyclealkyl**;

D is selected from the group consisting of



wherein Z is selected from the group consisting of alkoxy, alkyl, amino, cyano, nitro,  $\text{CO}_2\text{P}_1$ ,  $\text{SO}_3\text{H}$ ,  $\text{PO}(\text{OH})_2$ ,  $\text{CH}_2\text{PO}(\text{OH})_2$ ,  $\text{CHFPO}(\text{OH})_2$ ,  $\text{CF}_2(\text{PO}(\text{OH})_2$ , **and**  $\text{C}(\text{=NH})\text{NH}_2$ ; **and the following 5-membered heterocycles:**



wherein  $\text{P}_1$  and  $\text{P}_2$  are independently selected from the group consisting of hydrogen, alkyl, alkenyl, arylalkyl, cycloalkyl and (cycloalkyl)alkyl;

$\text{R}_1$ ,  $\text{R}_2$ ,  $\text{R}_3$ ,  $\text{R}_4$  and  $\text{R}_5$  are independently selected from the group consisting of hydrogen, alkoxy, alkyl, aryl, arylalkyl, cyano, halo, haloalkoxy, haloalkyl, **heterocycle**, **heterocyclealkyl**, hydroxy, hydroxyalkyl, nitro,  $\text{NR}_\text{A}\text{R}_\text{B}$ ,  $\text{NR}_\text{A}\text{R}_\text{B}\text{C}(\text{O})$ ,  $\text{NR}_\text{A}\text{R}_\text{B}\text{C}(\text{O})\text{alkyl}$  and  $\text{NR}_\text{A}\text{R}_\text{B}\text{C}(\text{O})\text{alkenyl}$ , wherein  $\text{R}_\text{A}$  and  $\text{R}_\text{B}$  are independently selected from the group consisting of hydrogen, alkyl, alkoxy carbonyl, alkylsulfonyl, aryl, arylalkyl carbonyl, aryl carbonyl, arylsulfonyl and  $(\text{R}_\text{C}\text{R}_\text{D}\text{N})\text{carbonyl}$  wherein  $\text{R}_\text{C}$  and  $\text{R}_\text{D}$  are independently selected from the group consisting of hydrogen, alkyl, aryl, and arylalkyl, **or  $\text{R}_\text{A}$  and  $\text{R}_\text{B}$  taken together with the nitrogen to which they are attached form a ring selected from the group consisting of pyrrolidine, piperidine, morpholine, homopiperidine and piperazine**;

$\text{L}$  is selected from the group consisting of  
 $-(\text{CH}_2)_\text{m}\text{X}_1(\text{CH}_2)_\text{n}\text{CH}(\text{R}_8)\text{C}(\text{R}_{9\text{A}})(\text{R}_{9\text{B}})\text{X}_2(\text{CH}_2)_\text{p}\text{C}(\text{O})\text{N}(\text{R}_{10})\text{CH}(\text{CO}_2\text{R}_{11})(\text{CH}_2)_\text{q}\text{X}_3-$ ;  
 $-(\text{CH}_2)_\text{m}\text{X}_1(\text{CH}_2)_\text{n}\text{CH}(\text{R}_8)\text{C}(\text{R}_{9\text{A}})(\text{R}_{9\text{B}})\text{X}_2(\text{CH}_2)_\text{p}\text{EC}(\text{O})\text{N}(\text{R}_{10})\text{CH}(\text{CO}_2\text{R}_{11})(\text{CH}_2)_\text{q}\text{X}_3-$ ;  
 $-(\text{CH}_2)_\text{m}\text{X}_1(\text{CH}_2)_\text{n}\text{CH}(\text{R}_8)\text{C}(\text{R}_{9\text{A}})(\text{R}_{9\text{B}})\text{X}_2(\text{CH}_2)_\text{p}\text{X}_3-$ ;  
 $-(\text{CH}_2)_\text{m}\text{X}_1(\text{CH}_2)_\text{n}\text{CH}(\text{R}_8)\text{C}(\text{R}_{9\text{A}})(\text{R}_{9\text{B}})\text{X}_2(\text{CH}_2)_\text{p}\text{X}_3(\text{CH}_2)_\text{q}\text{X}_4-$ ; and

$-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pE(CH_2)_qX_3-$ , wherein each group is drawn with the left end attached to A and the right end attached to B;

m, n, p and q are independently between 0-4;

$R_8$  is selected from the group consisting of hydrogen, hydroxy,  $NR_AR_B$  and  $(NR_AR_B)alkyl$ ;

$R_{9A}$  and  $R_{9B}$  are independently selected from the group consisting of hydrogen, alkyl, hydroxyalkyl and  $R_ER_FNalkyl$ , wherein  $R_E$  and  $R_F$  are independently selected from the group consisting of hydrogen, alkyl, alkoxy carbonyl and alkanoyl, or  $R_{9A}$  and  $R_{9B}$  taken together are oxo;

$R_{10}$  is selected from the group consisting of hydrogen, alkyl, alkanoyl and alkoxy carbonyl;

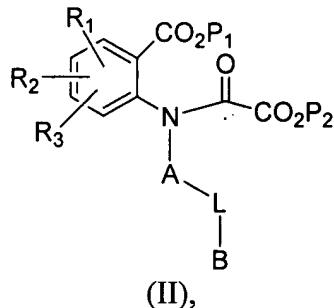
$R_{11}$  is independently selected from the group consisting of hydrogen, alkyl, alkenyl, arylalkyl, cycloalkyl, and (cycloalkyl)alkyl;

E is selected from the group consisting of aryl and cycloalkyl;

$X_1$ ,  $X_2$ ,  $X_3$ , and  $X_4$  are independently absent or are independently selected from the group consisting of  $NR_G$ , O, S,  $S(O)$  and  $S(O)_2$ , wherein  $R_G$  is selected from the group consisting of hydrogen, alkyl, alkanoyl and alkoxy carbonyl; and

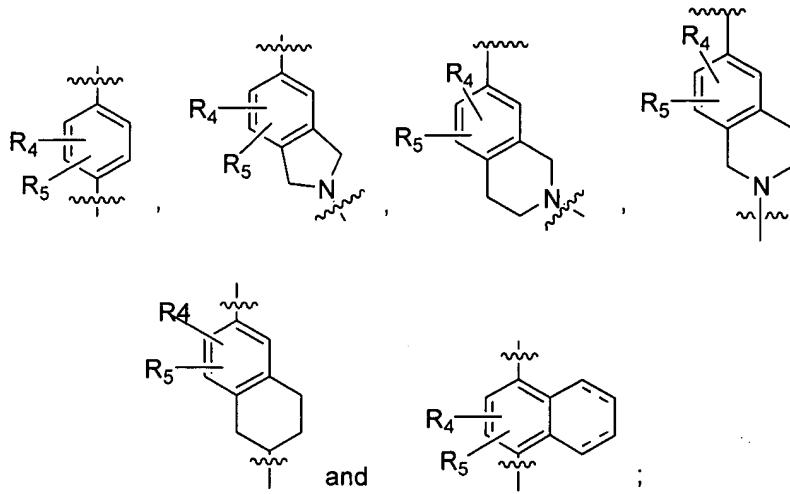
$W_1$ ,  $W_2$ ,  $W_3$  and  $W_4$  are independently selected from the group consisting of CH,  $CH_2$ , N, NH and O.

2 (Original). The compound according to claim 1 of formula (II)



or a therapeutically acceptable salt or prodrug thereof wherein A, B, L,  $P_1$ ,  $P_2$ ,  $R_1$ ,  $R_2$ , and  $R_3$  are defined in Claim 1.

3 (Currently Amended). The compound according to claim 2, wherein A is selected from the group consisting of



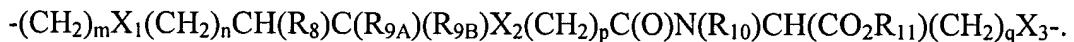
R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are independently selected from the group consisting of hydrogen, alkoxy, alkyl, cyano, halo, haloalkoxy, haloalkyl, **heterocycle**, hydroxy, hydroxyalkyl, nitro, NR<sub>A</sub>R<sub>B</sub>, NR<sub>A</sub>R<sub>B</sub>C(O), NR<sub>A</sub>R<sub>B</sub>C(O)alkyl and NR<sub>A</sub>R<sub>B</sub>C(O)alkenyl;

R<sub>10</sub> is selected from the group consisting of hydrogen and alkyl; and

R<sub>11</sub> is independently selected from the group consisting of hydrogen, alkyl and arylalkyl.

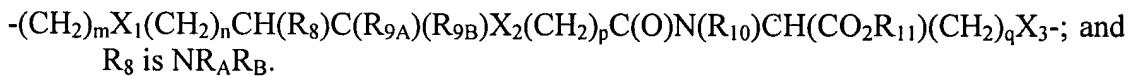
4 (Original). The compound according to claim 2, wherein

L is



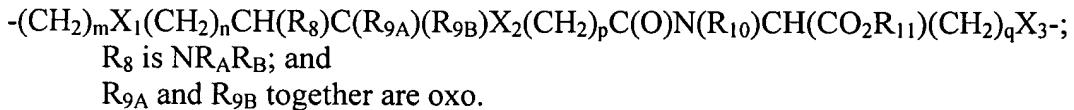
5 (Original). The compound according to claim 2, wherein

L is



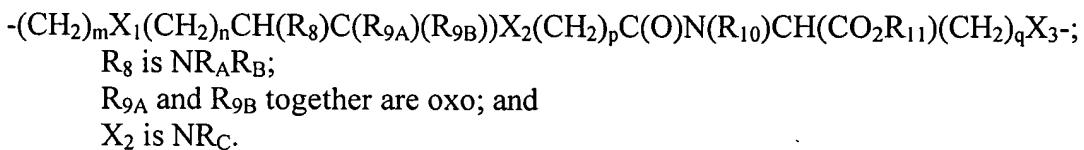
6 (Original). The compound according to claim 2, wherein

L is



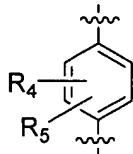
7 (Original). The compound according to claim 2, wherein

L is



8 (Currently Amended). The compound according to claim 2, wherein  
L is  
-(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>))X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>C(O)N(R<sub>10</sub>)CH(CO<sub>2</sub>R<sub>11</sub>)(CH<sub>2</sub>)<sub>q</sub>X<sub>3</sub>-;  
R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;  
R<sub>9A</sub> and R<sub>9B</sub> together are oxo;  
X<sub>2</sub> is NR<sub>C</sub>; and  
B is ~~selected from the group consisting of aryl and heterocycle~~.

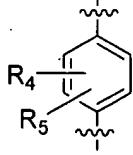
9 (Currently Amended). The compound according to claim 2, wherein  
L is  
-(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>))X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>C(O)N(R<sub>10</sub>)CH(CO<sub>2</sub>R<sub>11</sub>)(CH<sub>2</sub>)<sub>q</sub>X<sub>3</sub>-;  
R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;  
R<sub>9A</sub> and R<sub>9B</sub> together are oxo;  
X<sub>2</sub> is NR<sub>C</sub>;  
B is ~~selected from the group consisting of aryl and heterocycle~~; and  
A is



10 (Original). The compound according to claim 9, which is  
N-[5-(*{N*-acetyl-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-3-ethylphenylalanyl}amino)pentanoyl]-L-tyrosine.

11 (Original). The compound according to claim 2, wherein  
L is  
-(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>))X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>C(O)N(R<sub>10</sub>)CH(CO<sub>2</sub>R<sub>11</sub>)(CH<sub>2</sub>)<sub>q</sub>X<sub>3</sub>-;  
R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;  
R<sub>9A</sub> and R<sub>9B</sub> together are oxo;  
X<sub>2</sub> is NR<sub>C</sub>; and  
B is hydrogen.

12 (Original). The compound according to claim 2, wherein  
L is  
-(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>))X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>C(O)N(R<sub>10</sub>)CH(CO<sub>2</sub>R<sub>11</sub>)(CH<sub>2</sub>)<sub>q</sub>X<sub>3</sub>-;  
R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;  
R<sub>9A</sub> and R<sub>9B</sub> together are oxo;  
X<sub>2</sub> is NR<sub>C</sub>;  
B is hydrogen; and  
A is



13 (Original). The compound according to claim 12, which is

N-[5-(*{*N-acetyl-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-3-ethylphenylalanyl*}*amino)pentanoyl]-L-norleucine.

14 (Original). The compound according to claim 2, wherein

L is

$-(CH_2)_m X_1 (CH_2)_n CH(R_8) C(R_{9A})(R_{9B}) X_2 (CH_2)_p EC(O) N(R_{10}) CH(CO_2 R_{11}) (CH_2)_q X_3^-$ .

15 (Original). The compound according to claim 2, wherein

L is

$-(CH_2)_m X_1 (CH_2)_n CH(R_8) C(R_{9A})(R_{9B}) X_2 (CH_2)_p EC(O) N(R_{10}) CH(CO_2 R_{11}) (CH_2)_q X_3^-$ ; and  
R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>.

16 (Original). The compound according to claim 2, wherein

L is

$-(CH_2)_m X_1 (CH_2)_n CH(R_8) C(R_{9A})(R_{9B}) X_2 (CH_2)_p EC(O) N(R_{10}) CH(CO_2 R_{11}) (CH_2)_q X_3^-$ ;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>; and

R<sub>9A</sub> and R<sub>9B</sub> together are oxo.

17 (Original). The compound according to claim 2, wherein

L is

$-(CH_2)_m X_1 (CH_2)_n CH(R_8) C(R_{9A})(R_{9B}) X_2 (CH_2)_p EC(O) N(R_{10}) CH(CO_2 R_{11}) (CH_2)_q X_3^-$ ;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;

R<sub>9A</sub> and R<sub>9B</sub> together are oxo; and

X<sub>2</sub> is NR<sub>C</sub>.

18 (Original). The compound according to claim 2, wherein

L is

$-(CH_2)_m X_1 (CH_2)_n CH(R_8) C(R_{9A})(R_{9B}) X_2 (CH_2)_p EC(O) N(R_{10}) CH(CO_2 R_{11}) (CH_2)_q X_3^-$ ;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;

R<sub>9A</sub> and R<sub>9B</sub> together are oxo;

X<sub>2</sub> is NR<sub>C</sub>; and

B is hydrogen.

19 (Original). The compound according to claim 2, wherein

L is

$-(CH_2)_m X_1 (CH_2)_n CH(R_8) C(R_{9A})(R_{9B}) X_2 (CH_2)_p EC(O) N(R_{10}) CH(CO_2 R_{11}) (CH_2)_q X_3^-$ ;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;

R<sub>9A</sub> and R<sub>9B</sub> together are oxo;

X<sub>2</sub> is NR<sub>C</sub>;

B is hydrogen; and

E is cycloalkyl.

20 (Original). The compound according to claim 2, wherein

L is

$-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pEC(O)N(R_{10})CH(CO_2R_{11})(CH_2)_qX_3-$ ;

$R_8$  is  $NR_AR_B$ ;

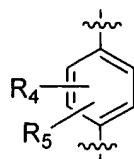
$R_{9A}$  and  $R_{9B}$  together are oxo;

$X_2$  is  $NR_C$ ;

$B$  is hydrogen;

$E$  is cycloalkyl; and

$A$  is



21 (Original). The compound according to claim 20, which is

$N\{-[4-(\{[N\text{-}acetyl-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-3-(2\text{-}hydroxyethyl)phenylalanyl]amino\}methyl]cyclohexyl\}carbonyl\}\text{-}L\text{-}norleucine$ .

22 (Original). The compound according to claim 2, wherein

$L$  is

$-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pC(O)N(R_{10})CH(CO_2R_{11})(CH_2)_qX_3-$ ;

$R_8$  is  $NR_AR_B$ ;

$R_{9A}$  and  $R_{9B}$  together are oxo;

$X_2$  is  $NR_C$ ;

$X_3$  is  $S$ ; and

$B$  is alkyl.

23 (Original). The compound according to claim 2, wherein

$L$  is

$-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pC(O)N(R_{10})CH(CO_2R_{11})(CH_2)_qX_3-$ ;

$R_8$  is  $NR_AR_B$ ;

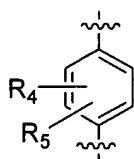
$R_{9A}$  and  $R_{9B}$  together are oxo;

$X_2$  is  $NR_C$ ;

$X_3$  is  $S$ ;

$B$  is alkyl; and

$A$  is



24 (Original). The compound according to claim 23, selected from the group consisting of

$N\{-5\text{-(}N\text{-}acetyl-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-3\text{-}ethylphenylalanyl]amino\}\text{-}pentanoyl\}\text{-}L\text{-}methionine$ ;

$methyl\ N\{-5\text{-(}N\text{-}acetyl-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-3\text{-}ethylphenylalanyl]amino\}\text{-}pentanoyl\}\text{-}L\text{-}methioninate$ ;

*N*-{5-[*N*-acetyl-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-3-ethylphenylalanyl]amino]pentanoyl}-*S*-ethyl-L-homocysteine;

*N*-{5-[*N*-acetyl-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-3-isopropylphenylalanyl]amino]pentanoyl}-L-methionine;

*N*-{5-[*N*-acetyl-4-[(carboxycarbonyl)(2-carboxy-5-chlorophenyl)amino]-3-ethylphenylalanyl]amino]pentanoyl}-L-methionine; and

*N*-(5-{[*N*-acetyl-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-3-(2-hydroxyethyl)phenylalanyl]amino} pentanoyl)-L-methionine.

25 (Original). The compound according to claim 2, wherein

L is

-(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>))X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>C(O)N(R<sub>10</sub>)CH(CO<sub>2</sub>R<sub>11</sub>)(CH<sub>2</sub>)<sub>q</sub>X<sub>3</sub>-;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;

R<sub>9A</sub> and R<sub>9B</sub> together are oxo;

X<sub>2</sub> is NR<sub>C</sub>;

X<sub>3</sub> is S; and

B is aryl.

26 (Original). The compound according to claim 2, wherein

L is

-(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>))X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>C(O)N(R<sub>10</sub>)CH(CO<sub>2</sub>R<sub>11</sub>)(CH<sub>2</sub>)<sub>q</sub>X<sub>3</sub>-;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;

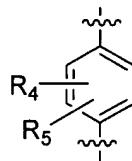
R<sub>9A</sub> and R<sub>9B</sub> together are oxo;

X<sub>2</sub> is NR<sub>C</sub>;

X<sub>3</sub> is S;

B is aryl; and

A is



27 (Original). The compound according to claim 26, which is

*N*-{5-[*N*-acetyl-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-3-ethylphenylalanyl]amino]pentanoyl}-*S*-benzyl-L-cysteine.

28 (Original). The compound according to claim 2, wherein

L is

-(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>))X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>C(O)N(R<sub>10</sub>)CH(CO<sub>2</sub>R<sub>11</sub>)(CH<sub>2</sub>)<sub>q</sub>X<sub>3</sub>-;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;

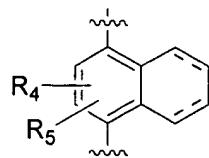
R<sub>9A</sub> and R<sub>9B</sub> together are oxo;

X<sub>2</sub> is NR<sub>C</sub>;

X<sub>3</sub> is S;

B is alkyl; and

A is



29 (Original). The compound according to claim 28, which is

*N*-(5-{[3-(4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-1-naphthyl)-N-(methoxycarbonyl)alanyl]amino}pentanoyl)-L-methionine.

30 (Original). The compound according to claim 2, wherein

L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>-.

31 (Original). The compound according to claim 2, wherein

L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>-; and

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>.

32 (Original). The compound according to claim 2, wherein

L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>-;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>; and

R<sub>9A</sub> and R<sub>9B</sub> together are oxo.

33 (Original). The compound according to claim 2, wherein

L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>-;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;

R<sub>9A</sub> and R<sub>9B</sub> together are oxo; and

X<sub>2</sub> is NR<sub>C</sub>.

34 (Original). The compound according to claim 2, wherein

L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>-;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;

R<sub>9A</sub> and R<sub>9B</sub> together are oxo;

X<sub>2</sub> is NR<sub>C</sub>; and

X<sub>3</sub> is O.

35 (Original). The compound according to claim 2, wherein

L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>-;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;

R<sub>9A</sub> and R<sub>9B</sub> together are oxo;

X<sub>2</sub> is NR<sub>C</sub>;

X<sub>3</sub> is O; and

B is aryl.

36 (Original). The compound according to claim 2, wherein

L is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3-$ ;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;

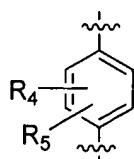
R<sub>9A</sub> and R<sub>9B</sub> together are oxo;

X<sub>2</sub> is NR<sub>C</sub>;

X<sub>3</sub> is O;

B is aryl; and

A is



37 (Original). The compound according to claim 36, selected from the group consisting of

methyl 2-[4-({N-[(allyloxy)carbonyl]-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-L-phenylalanyl}amino)butoxy]-6-hydroxybenzoate;

methyl 2-[4-[(N-acetyl-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-3-ethylphenylalanyl}amino]butoxy]-6-hydroxybenzoate;

methyl 4-{4-[(N-acetyl-4-amino-3-ethylphenylalanyl)amino]butoxy}-2-hydroxy-1,1'-biphenyl-3-carboxylate;

2-[4-({N-acetyl-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-3-ethylphenylalanyl}amino)butoxy]-6-hydroxybenzoic acid;

methyl 6-{4-[(N-acetyl-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-3-ethylphenylalanyl}amino]butoxy}-3-bromo-2-hydroxybenzoate;

methyl 2-(4-{[4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-N-(methoxycarbonyl)-L-phenylalanyl}amino)butoxy)-6-hydroxy-4-pentylbenzoate;

methyl 2-(4-{[4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-N-(methoxycarbonyl)-L-phenylalanyl}amino)butoxy)-6-hydroxy-4-methoxybenzoate;

methyl 3-(4-{[4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-N-(methoxycarbonyl)-L-phenylalanyl}amino)butoxy)-5-hydroxy-1,1'-biphenyl-4-carboxylate;

methyl 2-(4-{[4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-N-(methoxycarbonyl)-L-phenylalanyl}amino)butoxy)-6-hydroxy-4-methylbenzoate;

methyl 2-(4-{[4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-N-(methoxycarbonyl)-L-phenylalanyl}amino)butoxy)-4-chloro-6-hydroxybenzoate;

methyl 2-(4-{[4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-N-(methoxycarbonyl)-L-phenylalanyl}amino)butoxy)-6-hydroxybenzoate;

4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-N-{4-[2-(aminocarbonyl)-3-hydroxyphenoxy]butyl}-N-(methoxycarbonyl)-L-phenylalaninamide;

methyl 3-(4-{[4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-N-(methoxycarbonyl)-L-phenylalanyl}amino)butoxy)-1-hydroxy-2-naphthoate;

4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-N-(4-{3-hydroxy-2-[(methylamino)carbonyl]phenoxy}butyl)-N-(methoxycarbonyl)-L-phenylalaninamide;

4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-*N*-(4-{2-[(ethylamino)carbonyl]-3-hydroxyphenoxy}butyl)-*N*-(methoxycarbonyl)-L-phenylalaninamide;  
*N*-{4-[2-(acetylamino)-3-hydroxyphenoxy]butyl}-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-*N*-(methoxycarbonyl)-L-phenylalaninamide; and  
4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-*N*-(4-{2-[(dimethylamino)carbonyl]-3-hydroxyphenoxy}butyl)-*N*-(methoxycarbonyl)-L-phenylalaninamide.

38 (Original). The compound according to claim 2, wherein

*L* is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3-$ ;

*R*<sub>8</sub> is *NR*<sub>A</sub>*R*<sub>B</sub>;

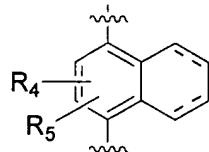
*R*<sub>9A</sub> and *R*<sub>9B</sub> together are oxo;

*X*<sub>2</sub> is *NR*<sub>C</sub>;

*X*<sub>3</sub> is O;

*B* is aryl; and

*A* is



39 (Original). The compound according to claim 38, selected from the group consisting of

methyl 2-[(5-{{[N\text{-}acetyl-3-(4-amino-1-naphthyl)-L-alanyl]amino}pentyl}oxy]-6-hydroxy-4-methylbenzoate; and

3-({5-{{[N\text{-}acetyl-3-(4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-1-naphthyl)-L-alanyl]amino}pentyl}oxy)-2-naphthoic acid.

40 (Original). The compound according to claim 2, wherein

*L* is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3-$ ; and

*R*<sub>8</sub> is hydrogen.

41 (Original). The compound according to claim 2, wherein

*L* is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3-$ ;

*R*<sub>8</sub> is hydrogen; and

*R*<sub>9A</sub> and *R*<sub>9B</sub> together are oxo.

42 (Original). The compound according to claim 2, wherein

*L* is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3-$ ;

*R*<sub>8</sub> is hydrogen;

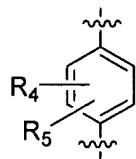
*R*<sub>9A</sub> and *R*<sub>9B</sub> together are oxo; and

*X*<sub>2</sub> is *NR*<sub>C</sub>.

43 (Original). The compound according to claim 2, wherein  
L is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3-$ ;  
R<sub>8</sub> is hydrogen;  
R<sub>9A</sub> and R<sub>9B</sub> together are oxo;  
X<sub>2</sub> is NR<sub>C</sub>; and  
X<sub>3</sub> is O.

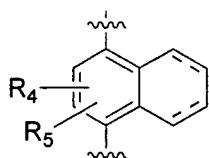
44 (Original). The compound according to claim 2, wherein  
L is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3-$ ;  
R<sub>8</sub> is hydrogen;  
R<sub>9A</sub> and R<sub>9B</sub> together are oxo;  
X<sub>2</sub> is NR<sub>C</sub>;  
X<sub>3</sub> is O; and  
B is aryl.

45 (Original). The compound according to claim 2, wherein  
L is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3-$ ;  
R<sub>8</sub> is hydrogen;  
R<sub>9A</sub> and R<sub>9B</sub> together are oxo;  
X<sub>2</sub> is NR<sub>C</sub>;  
X<sub>3</sub> is O; and  
B is aryl; and  
A is



46 (Original). The compound according to claim 45, which is  
methyl 2-{4-{{3-[(4-[(carboxy carbonyl)(2-carboxyphenyl)amino]-3-ethylphenyl)propanoyl]amino}butoxy}-6-hydroxybenzoate.

47 (Original). The compound according to claim 2, wherein  
L is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3-$ ;  
R<sub>8</sub> is hydrogen;  
R<sub>9A</sub> and R<sub>9B</sub> together are oxo;  
X<sub>2</sub> is NR<sub>C</sub>;  
X<sub>3</sub> is O;  
B is aryl; and  
A is



48 (Original). The compound according to claim 47, which is

2-((carboxycarbonyl){4-[3-(4-[3-hydroxy-2-(methoxycarbonyl)phenoxy]butyl}amino)-3-oxopropyl]-[(carboxycarbonyl)(2-carboxyphenyl)amino]-1-naphthyl}amino)benzoic acid.

49 (Original). The compound according to claim 2, wherein

L is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3-$ ;

R<sub>8</sub> is hydrogen; and

R<sub>9A</sub> is alkyl.

50 (Original). The compound according to claim 2, wherein

L is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3-$ ;

R<sub>8</sub> is hydrogen;

R<sub>9A</sub> is alkyl; and

X<sub>2</sub> is NR<sub>C</sub>.

51 (Original). The compound according to claim 2, wherein

L is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3-$ ;

R<sub>8</sub> is hydrogen;

R<sub>9A</sub> is alkyl;

X<sub>2</sub> is NR<sub>C</sub>; and

X<sub>3</sub> is O.

52 (Original). The compound according to claim 2, wherein

L is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3-$ ;

R<sub>8</sub> is hydrogen;

R<sub>9A</sub> is alkyl;

X<sub>2</sub> is NR<sub>C</sub>;

X<sub>3</sub> is O; and

B is aryl.

53 (Original). The compound according to claim 2, wherein

L is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3-$ ;

R<sub>8</sub> is hydrogen;

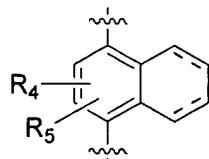
R<sub>9A</sub> is alkyl;

X<sub>2</sub> is NR<sub>C</sub>;

X<sub>3</sub> is O;

B is aryl; and

A is



54 (Original). The compound according to claim 53, which is methyl 2-(4-{[3-(4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-1-naphthyl)-1-methylpropyl]amino}butoxy)-6-hydroxybenzoate.

55 (Original). The compound according to claim 2, wherein  
L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>-;  
R<sub>8</sub> is hydrogen; and  
R<sub>9A</sub> and R<sub>9B</sub> are both hydrogen.

56 (Original). The compound according to claim 2, wherein  
L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>-;  
R<sub>8</sub> is hydrogen;  
R<sub>9A</sub> and R<sub>9B</sub> are both hydrogen; and  
X<sub>2</sub> is NR<sub>C</sub>.

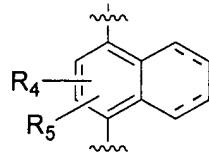
57 (Original). The compound according to claim 2, wherein  
L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>-;  
R<sub>8</sub> is hydrogen;  
R<sub>9A</sub> and R<sub>9B</sub> are both hydrogen;  
X<sub>2</sub> is NR<sub>C</sub>; and  
X<sub>3</sub> is O.

58 (Original). The compound according to claim 2, wherein  
L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>-;  
R<sub>8</sub> is hydrogen;  
R<sub>9A</sub> and R<sub>9B</sub> are both hydrogen;  
X<sub>2</sub> is NR<sub>C</sub>;  
X<sub>3</sub> is O; and  
B is aryl.

59 (Original). The compound according to claim 2, wherein  
L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>-;  
R<sub>8</sub> is hydrogen;  
R<sub>9A</sub> and R<sub>9B</sub> are both hydrogen;  
X<sub>2</sub> is NR<sub>C</sub>;

X<sub>3</sub> is O;  
B is aryl; and

A is



60 (Original). The compound according to claim 59, which is methyl 2-(4-{[3-(4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-1-naphthyl)propyl]amino}butoxy)-6-hydroxybenzoate.

61 (Original). The compound according to claim 2, wherein

L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>(CH<sub>2</sub>)<sub>q</sub>X<sub>4</sub>-.

62 (Original). The compound according to claim 2, wherein

L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>(CH<sub>2</sub>)<sub>q</sub>X<sub>4</sub>-; and

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>.

63 (Original). The compound according to claim 2, wherein

L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>(CH<sub>2</sub>)<sub>q</sub>X<sub>4</sub>-;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>; and

R<sub>9A</sub> and R<sub>9B</sub> together are oxo.

64 (Original). The compound according to claim 2, wherein

L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>(CH<sub>2</sub>)<sub>q</sub>X<sub>4</sub>-;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;

R<sub>9A</sub> and R<sub>9B</sub> together are oxo; and

X<sub>2</sub> is NR<sub>C</sub>.

65 (Original). The compound according to claim 2, wherein

L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>(CH<sub>2</sub>)<sub>q</sub>X<sub>4</sub>-;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;

R<sub>9A</sub> and R<sub>9B</sub> together are oxo;

X<sub>2</sub> is NR<sub>C</sub>; and

X<sub>3</sub> is O.

66 (Original). The compound according to claim 2, wherein

L is -(CH<sub>2</sub>)<sub>m</sub>X<sub>1</sub>(CH<sub>2</sub>)<sub>n</sub>CH(R<sub>8</sub>)C(R<sub>9A</sub>)(R<sub>9B</sub>)X<sub>2</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>3</sub>(CH<sub>2</sub>)<sub>q</sub>X<sub>4</sub>-;

R<sub>8</sub> is NR<sub>A</sub>R<sub>B</sub>;

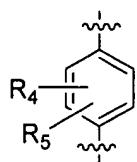
$R_{9A}$  and  $R_{9B}$  together are oxo;  
 $X_2$  is  $NR_C$ ;  
 $X_3$  is O; and  
 $X_4$  is O.

67 (Original). The compound according to claim 2, wherein

L is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3(CH_2)_qX_4-$ ;  
 $R_8$  is  $NR_AR_B$ ;  
 $R_{9A}$  and  $R_{9B}$  together are oxo;  
 $X_2$  is  $NR_C$ ;  
 $X_3$  is O;  
 $X_4$  is O; and  
B is aryl.

68 (Original). The compound according to claim 2, wherein

L is  $-(CH_2)_mX_1(CH_2)_nCH(R_8)C(R_{9A})(R_{9B})X_2(CH_2)_pX_3(CH_2)_qX_4-$ ;  
 $R_8$  is  $NR_AR_B$ ;  
 $R_{9A}$  and  $R_{9B}$  together are oxo;  
 $X_2$  is  $NR_C$ ;  
 $X_3$  is O;  
 $X_4$  is O;  
B is aryl; and  
A is



69 (Original). The compound according to claim 68, which is

methyl 2-{2-[2-({N-[(allyloxy)carbonyl]-4-[(carboxycarbonyl)(2-carboxyphenyl)amino]-L-phenylalanyl}amino)ethoxy]ethoxy}-6-hydroxybenzoate;

70 (Original). A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 in combination with a pharmaceutically acceptable carrier.

71 (Currently Amended). A method of ~~method of~~ **treating diabetes by** selectively inhibiting protein tyrosine phosphatase 1B comprising administering a therapeutically effective amount of a compound of claim 1.

72 (Currently Amended). A method of treating **diabetes disorders** caused by overexpressed or altered protein tyrosine phosphatase 1B comprising administering a therapeutically effective amount of a compound of claim 1.

73 (Canceled). The method of claim 72, wherein the disorder is type I and type II diabetes.

74 (Canceled). The method of claim 72, wherein the disorder is obesity.

75 (Canceled). A method of claim 72, wherein the disorder is autoimmune disorders, acute and chronic inflammatory disorders, osteoporosis, cancer, malignant disorders.

## **RESPONSE**

Applicants have amended the claims to reflect the election of group I made on 2/21/03. All claimed limitations related to heterocyclic compounds have been removed from the claims. Applicants respectfully maintain that claims 1-70 are now in condition for allowance.

Claims 71-75 stand rejected under 35 U.S.C. 112, first paragraph. Examiner maintains that the specification is not enabling for the claims directed to treating disorders caused by overexpressed or altered protein tyrosine phosphatase 1B. The Examiner maintains that the claims are not directed to specific diseases, but all kinds of diseases that use the mechanistic nature of inhibiting protein tyrosine phosphatase 1B. Applicants respectfully traverse this rejection and request withdrawal of the same.

Applicants have amended claims 71 and 72 to specify a disease treatable by inhibiting protein tyrosine phosphatase 1B. Claims 73-75 have been canceled. Applicants respectfully maintain that amended claims 71 and 72 are now in condition for allowance.

## **ACTION REQUESTED**

For all the forgoing reasons, Applicants submit that Claims 1-72 are in condition for allowance. To that end, the examiner is invited to contact the undersigned to schedule an Examiner Interview to discuss any matter.

Respectfully submitted,  
Liu, *et al.*



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